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 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2          "Ask CAS" for self-help around the clock
 NEWS  3  AUG 09  INSPEC enhanced with 1898-1968 archive
 NEWS  4  AUG 28  ADISCTI Reloaded and Enhanced
 NEWS  5  AUG 30  CA(SM)/CAplus(SM) Austrian patent law changes
 NEWS  6  SEP 11  CA/CAplus enhanced with more pre-1907 records
 NEWS  7  SEP 21  CA/CAplus fields enhanced with simultaneous left and right
                  truncation
 NEWS  8  SEP 25  CA(SM)/CAplus(SM) display of CA Lexicon enhanced
 NEWS  9  SEP 25  CAS REGISTRY(SM) no longer includes Concord 3D coordinates
 NEWS 10  SEP 25  CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
 NEWS 11  SEP 28  CEABA-VTB classification code fields reloaded with new
                  classification scheme
 NEWS 12  OCT 19  LOGOFF HOLD duration extended to 120 minutes
 NEWS 13  OCT 19  E-mail format enhanced
 NEWS 14  OCT 23  Option to turn off MARPAT highlighting enhancements available
 NEWS 15  OCT 23  CAS Registry Number crossover limit increased to 300,000 in
                  multiple databases
 NEWS 16  OCT 23  The Derwent World Patents Index suite of databases on STN
                  has been enhanced and reloaded
 NEWS 17  OCT 30  CHEMLIST enhanced with new search and display field
 NEWS 18  NOV 03  JAPIO enhanced with IPC 8 features and functionality

 NEWS EXPRESS  JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
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 NEWS IPC8     For general information regarding STN implementation of IPC 8
 NEWS X25      X.25 communication option no longer available

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=> fil reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     1.05       1.05
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DICTIONARY FILE UPDATES: 8 NOV 2006 HIGHEST RN 912757-80-3

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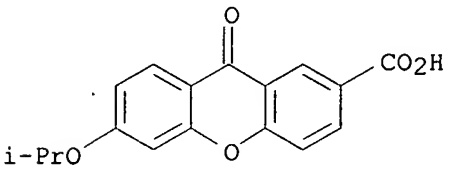
http://www.cas.org/ONLINE/UG/regprops.html

=> s AH 6809/cn
L1 1 AH 6809/CN

=> d

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN
RN 33458-93-4 REGISTRY
ED Entered STN: 16 Nov 1984
CN 9H-Xanthene-2-carboxylic acid, 6-(1-methylethoxy)-9-oxo- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Xanthene-2-carboxylic acid, 6-isopropoxy-9-oxo- (8CI)
OTHER NAMES:
CN 6-Isopropoxy-9-oxoxanthene-2-carboxylic acid
CN AH 6809
MF C17 H14 O5
LC STN Files: AGRICOLA, BIOSIS, BIOTECHNO, CA, CAPLUS, CHEMCATS, CIN, CSCHEM, EMBASE, IFICDB, IFIPAT, IFIUDB, MEDLINE, PHAR, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

32 REFERENCES IN FILE CA (1907 TO DATE)
32 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> sel rn name
E1 THROUGH E3 ASSIGNED

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=> fil hcapl
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         7.50       8.55

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FILE LAST UPDATED: 8 Nov 2006  (20061108/ED)

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=> fil medl hcapl biosis uspatf wpids
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         2.53      11.08

FILE 'MEDLINE' ENTERED AT 14:55:26 ON 09 NOV 2006

FILE 'HCAPLUS' ENTERED AT 14:55:26 ON 09 NOV 2006
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FILE 'WPIDS' ENTERED AT 14:55:26 ON 09 NOV 2006
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=> s e1-3
L2          373 ("AH 6809"/BI OR 33458-93-4/BI OR "6-ISOPROPOXY-9-OXOXANTHENE-2-
                CARBOXYLIC ACID"/BI)

=> s contracept?
L3       122252 CONTRACEPT?

=> s l2 and l3
L4            5 L2 AND L3

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5            4 DUP REM L4 (1 DUPLICATE REMOVED)

=> d ibib abs tot
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L5 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2004:252196 HCAPLUS
DOCUMENT NUMBER: 140:247120
TITLE: EP2 receptor antagonists and selective COX-2 inhibitors for female oral contraception
INVENTOR(S): Lindenthal, Bernhard; Buchmann, Bernd; Skuballa, Werner; Hegele-Hartung, Christa
PATENT ASSIGNEE(S): Schering Ag, Germany
SOURCE: U.S. Pat. Appl. Publ., 17 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004058975	A1	20040325	US 2003-606289		20030626
PRIORITY APPLN. INFO.:			GB 2002-14802	A	20020626
			US 2002-414363P	P	20020930

AB The present invention relates to a method for impairing cumulus expansion and oocyte maturation, the method comprising antagonizing EP2 receptor and/or inhibiting cyclooxygenase COX-2. The invention also relates to the use of a pharmaceutical composition comprising an EP 2 receptor antagonist (optionally with one or more COX inhibitors) for female contraception.

L5 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:855825 HCAPLUS
DOCUMENT NUMBER: 139:354462
TITLE: FP receptor antagonists or PGF2α antagonists for treating menorrhagia
INVENTOR(S): Jabbour, Henry Nicolas; Critchley, Hilary Octavia Dawn
PATENT ASSIGNEE(S): Medical Research Council, UK
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003089002	A1	20031030	WO 2003-GB1536		20030410
WO 2003089002	C2	20041223			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2003219327	A1	20031103	AU 2003-219327		20030410
EP 1494715	A1	20050112	EP 2003-715136		20030410
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP 2005532295	T2	20051027	JP 2003-585753		20030410
US 2006166872	A1	20060727	US 2005-511484		20051021
PRIORITY APPLN. INFO.:			GB 2002-8783	A	20020417
			GB 2002-8785	A	20020417
			WO 2003-GB1536	W	20030410

AB A method of treating or preventing menorrhagia in a female individual comprising administering to the individual at least one agent that prevents PGF2α having its effect on the prostaglandin FP receptor. Optionally, an inhibitor of prostaglandin endoperoxide synthase (PGES) and/or an antagonist of EP2 or EP4 is also administered. For example, a patient with menorrhagia was treated with a FP receptor antagonist AL-3138 or AL-8810 at a dosing and frequency such that the therapeutic level of active agents at the site of treatment is maintained at a level ideally EC90 but preferably not less than EC50 throughout the treatment period. The treatment was delivered orally or more locally depending on patient acceptability, avoidance of side effects, and systemic bioavailability.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:855824 HCAPLUS
DOCUMENT NUMBER: 139:354461
TITLE: FP receptor antagonists or PGF2α antagonists for treating pathological conditions of the uterus
INVENTOR(S): Milne, Stuart Angus; Jabbour, Henry Nicolas
PATENT ASSIGNEE(S): Medical Research Council, UK
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003089001	A1	20031030	WO 2003-GB1521	20030410
WO 2003089001	C1	20040205		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003217066	A1	20031103	AU 2003-217066	20030410
EP 1511514	A1	20050309	EP 2003-712454	20030410
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005537225	T2	20051208	JP 2003-585752	20030410
PRIORITY APPLN. INFO.:			GB 2002-8785 A	20020417
			WO 2003-GB1521 W	20030410

AB A method of treating or preventing a pathol. condition of the uterus in a female individual comprises administering to the individual at least one agent that prevents PGF2α having its effect on the FP receptor. Typically, the pathol. condition is uterine cancer, fibroids or endometriosis. For example, a patient suffering from uterine cancer was administered a FP receptor antagonist AL-3138 or AL-8810 and an EP2 receptor antagonist AH-6809 at a dosing quantity and frequency such as that the therapeutic level of active agent at the site of treatment was maintained at a level ideally EC90 but preferably not less than EC50 throughout the treatment period. The treatment was delivered orally or more locally depending on patient acceptability, avoidance of side effects, and systemic bioavailability.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:930958 HCAPLUS
DOCUMENT NUMBER: 140:713
TITLE: Method of treating cervical cancer with an inhibitor of cyclooxygenase-1 or with EP2 or EP4 receptor antagonists
INVENTOR(S): Sales, Kurt Jason; Jabbour, Henry Nicolas; Katz, Arieh
PATENT ASSIGNEE(S): UK
SOURCE: U.S. Pat. Appl. Publ., 32 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2003220266	A1	20031127	US 2002-284569		20021030
PRIORITY APPLN. INFO.:			US 2001-340971P	P	20011030

AB A method of treating a neoplastic condition of the cervix in a patient the method comprising administering to the patient an inhibitor of cyclooxygenase-1 (COX-1) and/or an EP2 and/or EP4 receptor antagonist. Overexpression of COX-1 in HeLa cells was associated with enhanced expression of the angiogenic factors: basic fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF), angiopoietin-1 (Ang-1) and angiopoietin-2 (Ang-2). This upregulation of angiogenic factor expression was abolished by indomethacin.

=> s ep2
L6 4271 EP2

=> s fertility
L7 174076 FERTILITY

=> s l6 and l7
L8 63 L6 AND L7

=> s l6 (S) l7
L9 26 L6 (S) L7

=> d ibib abs 24-26

L9 ANSWER 24 OF 26 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-364268 [37] WPIDS
CROSS REFERENCE: 2005-417031; 2005-424502
DOC. NO. CPI: C2005-111853 [37]
TITLE: New 2-decarboxy-2-phosphinico prostaglandin derivatives are thrombaxane antagonists used for treating e.g. osteoporosis, erectile dysfunction, pain, hepatic diseases, renal diseases, pancreatitis, myocardial infarct, ulcers and glaucoma
DERWENT CLASS: B05
INVENTOR: DELONG M A
PATENT ASSIGNEE: (PROC-C) PROCTER & GAMBLE CO
COUNTRY COUNT: 1

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 6894175	B1	20050517	(200537)*	EN	49[0]	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE

US 6894175 B1 Provisional US 1999-158637P 19991008
US 6894175 B1 US 2000-633180 20000804

PRIORITY APPLN. INFO: US 2000-633180 20000804
US 1999-158637P 19991008
AN 2005-364268 [37] WPIDS
CR 2005-417031; 2005-424502
AB US 6894175 B1 UPAB: 20051222
NOVELTY - 2-Decarboxy-2-phosphinico prostaglandin derivatives (I)-(XXII), are new.

DETAILED DESCRIPTION - 2-Decarboxy-2-phosphinico prostaglandin derivatives of formula (I)-(XXII), are new.

Bond a = a single bond, a trans double bond or a triple bond;

Q1 = R5-P(=R4)(R1)R3-R2;

Q2 = CH2-R6-R7-R8;

R1 = H, 1-4C hydrocarbyl or 1-4 membered heterogenous group, where the member atom directly adjacent to P in the heterogenous group is not O;

R2 = hydrocarbyl, heterogeneous group, carbocyclyl, heterocyclyl, aryl or heteroaryl (all optionally substituted), mono- or poly-valent inorganic cation, mono- or poly-valent organic cation or H;

R3 = O, S or NH;

R4 = O or S;

R5 = divalent hydrocarbyl or heterogeneous group (both optionally substituted);

R6 = absent, CH2, C(O) or C(R10)OR10);

R7 = absent or (CD(D))p-X-(CD(D))q;

p, q = 0-3;

X = O, S, SO, SO2 or ND';

D' = H, 1-4C hydrocarbyl or 1-4 membered heterogenous group;

R8 = hydrocarbyl, heterogenous group, carbocyclyl, heterocyclyl, aryl or heteroaryl (all optionally substituted);

R9 = D', and

R14 = D' or halo, and

heterogenous group = straight or branched saturated or unsaturated 1-18 membered optionally saturated chain comprising at least carbon and one heteroatom.

ACTIVITY - Osteopathic; Vasotropic; Hypotensive; Endocrine-Gen.; Dermatological; Analgesic; Antiasthmatic; Antiarthritic; Gastrointestinal-Gen.; Hepatotropic; Nephrotropic; Antiinflammatory; Cardiant; Antiulcer; Gynecological; Ophthalmological; Respiratory-Gen.; Antiinfertility; Antidiabetic; Tocolytic; Antiallergic; Anticoagulant; Thrombolytic.

Tests are described, but no results are given.

MECHANISM OF ACTION - Prostanoid receptor (EP1-EP4) modulator; EP1 receptor modulator; EP3 receptor modulator; EP4 receptor modulator; Human prostanoid (FP) receptor modulator ;Prostaglandin agonist; Thrombaxane antagonist.

USE - Used to treat medical and cosmetic conditions, particularly as EP1 agonists (to treat bone disorders such as osteoporosis, vascular diseases such as high blood pressure and poor vascular circulation, sexual dysfunction such as erectile dysfunction and women's sexual arousal dysfunction); as prostaglandin E1 agonists (to enhance skin pigmentation); as EP1 antagonists (to treat pain); as EP2 agonists (to treat asthma and bone disorders such as osteoporosis, inhibit cell migration and protect against neuronal damage in eye and also to enhance skin pigmentation); as EP2 antagonists (has a diuretic effect and to treat hypertension and premenstrual tension); as EP3 agonists (to treat arthritis, bone disorders such as osteoporosis, vascular disease such as high blood pressure and poor vascular circulation, to enhance uterine contractions and inhibit gastric acid secretion, to prevent and/or treat hepatic diseases, renal diseases, pancreatitis, myocardial infarct and gastric disturbances such as ulcers); as EP3 antagonists (to control blood pressure); as EP4 antagonists (having a diuretic effect and to treat hypertension and premenstrual tension and to lower intraocular pressure to

treat conditions such as glaucoma); as FP agonists (to treat bone disorders such as osteoporosis, ocular disorders such as glaucoma, skin disorders, circulatory disorders such as hypertension, gastrointestinal disorders, hair loss, respiratory disorders, for fertility control, to manage vascular diseases such as diabetic and other forms of peripheral vascular disease, to induce labor and as nasal decongestants); as FP antagonists (to prevent premature labor and hyper-pigmentation of the skin); as IP agonists (treat vascular disorders such as peripheral vascular disease, pulmonary hypertension, high blood pressure and poor vascular circulation; reproductive disorders such as cervical immaturity, to inhibit uterine contractions and to prevent premature delivery); and as thromboxane antagonists (used as anti-allergy agents, to treat vascular disease and to prevent platelet coagulation).

L9 ANSWER 25 OF 26 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-268841 [25] WPIDS
DOC. NO. CPI: C2004-104607 [25]
TITLE: Impairment of cumulus expansion and oocyte maturation useful for controlling fertility in a woman comprises antagonizing the Prostaglandin type 2 receptor and/or inhibiting cyclooxygenase 2
DERWENT CLASS: B04
INVENTOR: BUCHMANN B; HEGELE-HARTUNG C; LINDENTHAL B; SKUBALLA W
PATENT ASSIGNEE: (SCHD-C) SCHERING AG
COUNTRY COUNT: 1

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 20040058975	A1	20040325	(200425)*	EN	17[4]	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 20040058975	A1 Provisional	US 2002-414363P	20020930
US 20040058975	A1	US 2003-606289	20030626

PRIORITY APPLN. INFO: GB 2002-14802 20020626
AN 2004-268841 [25] WPIDS
AB US 20040058975 A1 UPAB: 20050528
NOVELTY - Impairment of cumulus expansion and oocyte maturation comprising antagonizing the Prostaglandin type-2 (EP2) receptor and/or inhibiting cyclooxygenase 2 (COX-2), is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for fertility control in a woman comprising administering EP2 receptor antagonist and/or cyclooxygenase 2 (COX-2) inhibitor.

ACTIVITY - Antiinfertility.

Mice within the metestrus stage were stimulated with male urine/cage spread from male animals to proceed to the oestrus stage. Beginning with the stimulation, EP-2 receptor antagonist was dosed per orally. Vaginally smears were performed every day and animals in the oestrus stage were killed 24 hours later in the metestrus stage and the number of ovulated oocytes in the oviduct were determined. Blood collections were performed to evaluate hormones. The result showed that the EP-2 receptor antagonist prevents ovulation, impairs cumulus expansion and oocyte maturation and provides oocytes which, when released do not have the competence to be fertilized.

MECHANISM OF ACTION - Prostaglandin type-2 (EP2) receptor antagonist. Cyclooxygenase (COX-2) inhibitor.

No biological data given.

USE - The method is used for the impairment of cumulus expansion and oocyte maturation to control fertility in a woman (claimed). The composition comprising an EP2 receptor antagonist and/or

cyclooxygenase 2 (COX-2) inhibitor is also useful as a contraceptive agent.

ADVANTAGE - The EP-2 antagonist can impair cumulus expansion and oocyte maturation preventing ovulation completely or delaying release of an oocyte which can not have the competence to be fertilize, therefore, the pregnancy may be prevented. The EP-2 antagonist prevents oocyte maturation and subsequent fertilization without disruption of ovulation and of the normal menstrual cycle, therefore, the endogenous hormonal environment is maintained. The method provides a non-steroid hormone application that is an alternative to current conventional steroid oral contraceptive methods. The EP-2 antagonist blocks the oocyte function without interference of the productive hormonal milieu and the normal menstrual cycle, therefore, the oestrous cycle and ovulation is not affected, the hypothalamic pituitary ovarian axis should not be altered during EP-2 receptor antagonist administration in vivo.

L9 ANSWER 26 OF 26 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-513472 [48] WPIDS
DOC. NO. CPI: C2003-137405 [48]
TITLE: New substituted pyrazolidinone compounds useful for treating or preventing asthma and hypertension
DERWENT CLASS: B03
INVENTOR: ARALDI G L; LIAO Y; REDDY A P; ZHAO Z
PATENT ASSIGNEE: (ARAL-I) ARALDI G L; (ISTF-C) ARS APPLIED RES SYSTEMS HOLDING NV; (LIAO-I) LIAO Y; (REDD-I) REDDY A P; (ZHAO-I) ZHAO Z
COUNTRY COUNT: 100

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2003035064	A1	20030501	(200348)*	EN	53[0]	
EP 1439837	A1	20040728	(200449)	EN		
AU 2002340282	A1	20030506	(200460)	EN		
US 20040254233	A1	20041216	(200482)	EN		
JP 2005509632	W	20050414	(200527)	JA	88	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003035064	A1	WO 2002-US33964	20021023
US 20040254233	A1 Provisional	US 2001-336048P	20011023
AU 2002340282	A1	AU 2002-340282	20021023
EP 1439837	A1	EP 2002-778630	20021023
EP 1439837	A1	WO 2002-US33964	20021023
US 20040254233	A1	WO 2002-US33964	20021023
JP 2005509632	W	WO 2002-US33964	20021023
JP 2005509632	W	JP 2003-537631	20021023
US 20040254233	A1	US 2004-492910	20040416

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1439837	A1 Based on	WO 2003035064 A
AU 2002340282	A1 Based on	WO 2003035064 A
JP 2005509632	W Based on	WO 2003035064 A

PRIORITY APPLN. INFO: US 2001-336048P 20011023
US 2004-492910 20040416
AN 2003-513472 [48] WPIDS
AB WO 2003035064 A1 UPAB: 20060119
NOVELTY - Substituted pyrazolidinone compounds (I) are new.

DETAILED DESCRIPTION - Substituted pyrazolidinone compounds of formula (I) or their salts are new.

R1 and R2 = (hetero)alkyl, (hetero)alkenyl, (hetero)alkynyl, aralkyl, heteroarylalkyl or heteroalicyclicalkyl (all optionally substituted) or H;

R3 and R4 = (hetero)alkyl, (hetero)alkenyl, (hetero)alkynyl, carbocyclic aryl, heteroalicyclic, heteroaryl, (hetero)aralkyl, or heteroalicyclicalkyl (all optionally substituted); and

o and p = 0 - 2.

AN INDEPENDENT CLAIM is included for a compound of formula (I) where o+p is at least one for the treatment of undesired muscle contraction.

ACTIVITY - Gynecological; Analgesic; Antiasthmatic; Hypotensive; Antiinfertility; Endocrine-Gen.; Ophthalmological; Cardiant; Immunosuppressive; Osteopathic; Cytostatic; Antiinflammatory; Antirheumatic; Antiarthritic; Neuroprotective; Antipsoriatic; Antiulcer; Nephrotropic; Vasotropic; Virucide; Anti-HIV; CNS-Gen.; Antianginal; Cerebroprotective; Thrombolytic; Anticoagulant; Gastrointestinal-Gen.; Dermatological.

MECHANISM OF ACTION - Prostaglandin EP2 and/or EP4 receptor binder; Prostanoid-induced smooth muscle contraction inhibitor. 4-(2-(2-(4-(3-Bromophenyl)-3-hydroxybutyl)-5-oxopyrazolidin-1-yl)ethyl)benzoic acid (Ia) was tested for EP4 cAMP assay by using a cAMP-screen ELISA System. (Ia) showed an Ki value of 13 nM.

USE - For treating pre-term labor, dysmenorrhea, asthma, hypertension, infertility or a fertility disorder, sexual dysfunction, undesired blood clotting, destructive bone disease or disorder, preeclampsia, eclampsia, eosinophil disorder in female with late stage pregnancy and for control of cervical ripening, glaucoma, undesired bone loss, undesired muscle contraction, disease or disorder associated with the prostaglandin EP2 receptor in a mammal (e.g. female) suffering from or susceptible to infertility, or ovulatory disorder (all claimed). Also useful for treating congestive heart disease, tissue or transplant rejection, undesired platelet activities, male erectile dysfunction, associated fibrotic disease, female sexual arousal disorder, osteoporosis, Paget's disease, healing or replacement of bone grafts, inflammatory disease and autoimmune disease (e.g. rheumatoid arthritis, multiple sclerosis, psoriasis, inflammatory bowel disease, and ulcerative colitis), renal dysfunction (e.g. acute or chronic renal failure, glomerulonephritis, and uraemia), viral infections (e.g. HIV infections), sleep disorders, ulcers, and skin disease (e.g. ichthyosis), myocardial ischemia, myocardial infarction, unstable angina, stroke associated with thrombosis, peripheral arterial thrombosis, anticoagulation involving artificial organ, cardiac valves; and for medical implementation.

ADVANTAGE - (I) exhibits a Ki of at most 50 (preferably 10) microM in a standard EP2 receptor binding assay. The compound exhibits prostaglandin EP2 and/or EP4 receptor binding affinity and prostanoid induced smooth muscle contraction inhibitory activity.

=> d ibib abs 10-14

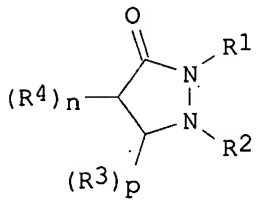
L9 ANSWER 10 OF 26 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	2003:334902 HCAPLUS
DOCUMENT NUMBER:	138:353975
TITLE:	Preparation of pyrazolidinones as ligands of the prostaglandin EP2 and/or EP4 receptors
INVENTOR(S):	Araldi, Gian Luca; Liao, Yihua; Reddy, Adulla P.; Zhao, Zhong
PATENT ASSIGNEE(S):	Applied Research Systems ARS Holding N.V., Neth. Antilles
SOURCE:	PCT Int. Appl., 106 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English

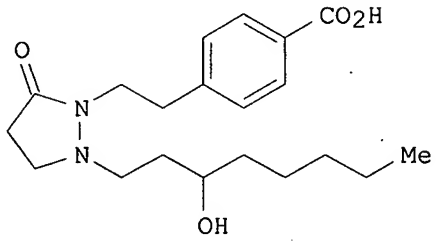
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003035064	A1	20030501	WO 2002-US33964		20021023
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2463102	AA	20030501	CA 2002-2463102		20021023
EP 1439837	A1	20040728	EP 2002-778630		20021023
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
JP 2005509632	T2	20050414	JP 2003-537631		20021023
US 2004254233	A1	20041216	US 2004-492910		20040416
PRIORITY APPLN. INFO.:			US 2001-336048P	P	20011023
			WO 2002-US33964	W	20021023

OTHER SOURCE(S): MARPAT 138:353975
GI



I



II

AB Title compds. I [wherein R1 and R2 = independently H or (un)substituted (hetero)alkyl, (hetero)alkenyl, (hetero)alkynyl, (hetero)arylalkyl, or heterocyclylalkyl; R3 and R4 = independently (un)substituted (hetero)alkyl, (hetero)alkenyl, (hetero)alkynyl, (hetero)aryl, (hetero)arylalkyl, or heterocyclyl(alkyl); n and p = independently 0-2; and pharmaceutically accept salts thereof] were prepared as prostaglandin EP2 and/or EP4 receptor ligands. For example, 4-(bromoethyl)benzoic acid was esterified with MeOH (98%), and the product coupled with t-Bu carbazate to give t-Bu 2-[2-(4-methoxycarbonylphenyl)ethyl]hydrazine (30%). Cyclization with 3-chloropropionyl chloride provided the t-Bu oxopyrazolidinecarboxylate (55%), which was deprotected using TFA (88%). Addition of 1-octen-3-one (72%) and subsequent reduction with CeCl3 and NaBH4 in EtOH afforded II (98%). In EP2 and EP4 receptor binding assays, the latter exhibited binding with Ki values of 2200 nM and 250 nM, resp. In total cAMP assays using HEK293-EBNA cells transfected with pCEP4-hEP2 and pCEP4-hEP4 receptors, II displayed activity with EC50 values of 595 nM and 5 nM, resp. Thus, I are useful for a variety of therapies, including treating or preventing preterm labor, dysmenorrhea, asthma, hypertension, infertility or fertility disorder, undesired blood clotting, preeclampsia or eclampsia, an eosinophil disorder, sexual dysfunction, osteoporosis and other destructive bone disease or disorder, and other diseases and disorders associated with the prostaglandin EP2 and/or

EP4 receptors (no data).
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 11 OF 26 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:552796 HCAPLUS
DOCUMENT NUMBER: 138:581
TITLE: Cloning and expression of the rabbit prostaglandin EP2 receptor
AUTHOR(S): Guan, Youfei; Stillman, Brett A.; Zhang, Yahua; Schneider, Andre; Saito, Osamu; Davis, Linda S.; Redha, Reyadh; Breyer, Richard M.; Breyer, Matthew D.
CORPORATE SOURCE: Division of Nephrolgy, Veterans Administration Medical Center, Vanderbilt University School of Medicine, Nashville, TN, 37232-2372, USA
SOURCE: BMC Pharmacology [online computer file] (2002), 2, No pp. given
CODEN: BPMHBU; ISSN: 1471-2210
URL: http://www.biomedcentral.com/1471-2210/2/14
PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background: Prostaglandin E2 (PGE2) has multiple physiol. roles mediated by G protein coupled receptors designated E-prostanoid, or "EP" receptors. Evidence supports an important role for the EP2 receptor in regulating fertility, vascular tone and renal function. Results: The full-length rabbit EP2 receptor cDNA was cloned. The encoded polypeptide contains 361 amino acid residues with seven hydrophobic domains. COS-1 cells expressing the cloned rabbit EP2 exhibited specific [3H]PGE2 binding with a Kd of 19.1±1.7 nM. [3H]PGE2 was displaced by unlabeled ligands in the following order: PGE2»PGD2=PGF2α=ilop rost. Binding of [3H]PGE2 was also displaced by EP receptor subtype selective agonists with a rank order of affinity consistent with the EP2 receptor (butaprost>AH13205>misoprostol>sulprostone). Butaprost free acid produced a concentration-dependent increase in cAMP accumulation in rabbit EP2 transfected COS-1 cells with a half-maximal effective concentration of 480 nM. RNase protection assay revealed high expression in the ileum, spleen, and liver with lower expression in the kidney, lung, heart, uterus, adrenal gland and skeletal muscle. In situ hybridization localized EP2 mRNA to the uterine endometrium, but showed no distinct localization in the kidney. EP2 mRNA expression along the endometrium, but showed no distinct localization in the kidney. EP2 mRNA expression along the nephron was determined by RT-PCR and its expression was present in glomeruli, MCD, tDL and CCD. In cultured cells EP2 receptor was not detected in collecting ducts but was detected in renal interstitial cells and vascular smooth muscle cells. EP2 mRNA was also detected in arteries, veins, and preglomerular vessels of the kidney. Conclusion: EP2 expression pattern is consistent with the known functional roles for cAMP coupled PGE2 effects in reproductive and vascular tissues and renal interstitial cells. It remains uncertain whether it is also expressed in renal tubules.
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 12 OF 26 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:633267 HCAPLUS
DOCUMENT NUMBER: 133:261912
TITLE: Growth differentiation factor-9 stimulates progesterone synthesis in granulosa cells via a prostaglandin E2/EP2 receptor pathway
AUTHOR(S): Elvin, Julia A.; Yan, Changning; Matzuk, Martin M.
CORPORATE SOURCE: Departments of Pathology, Molecular and Human Genetics, Baylor College of Medicine, Houston, TX, 77030, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2000), 97(18), 10288-10293

CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Growth differentiation factor-9 (GDF-9), an oocyte-secreted member of the transforming growth factor β superfamily, progesterone receptor, cyclooxygenase 2 (Cox2; Ptgs2), and the EP2 prostaglandin E2 (PGE2) receptor (EP2; Ptgerep2) are required for fertility in female but not male mice. To define the interrelationship of these factors, the authors used a preovulatory granulosa cell culture system in which the authors added recombinant GDF-9, prostaglandins, prostaglandin receptor agonists, or cyclooxygenase inhibitors. GDF-9 stimulated Cox-2 mRNA within 2 h, and PGE2 within 6 h; however, progesterone was not increased until 12 h after addition of GDF-9. This suggested that Cox2 is a direct downstream target of GDF-9 but that progesterone synthesis required an intermediate. To determine whether prostaglandin synthesis was required for progesterone production, the authors analyzed the effects of PGE2 and cyclooxygenase inhibitors on this process. PGE2 can stimulate progesterone synthesis by itself, although less effectively than GDF-9 (3-fold vs. 6-fold increase over 24 h, resp.). Furthermore, indomethacin or NS-398, inhibitors of Cox2, block basal and GDF-9-stimulated progesterone synthesis. However, addition of PGE2 to cultures containing both GDF-9 and NS-398 overrides the NS-398 block in progesterone synthesis. To further define the PGE2-dependent pathway, the authors show that butaprost, a specific EP2 agonist, stimulates progesterone synthesis and overrides the NS-398 block. In addition, GDF-9 stimulates EP2 mRNA synthesis by a prostaglandin- and progesterone-independent pathway. Thus, GDF-9 induces an EP2 signal transduction pathway which appears to be required for progesterone synthesis in cumulus granulosa cells. These studies further demonstrate the importance of oocyte-somatic cell interactions in female reproduction
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 13 OF 26 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:354321 HCAPLUS
DOCUMENT NUMBER: 133:99638
TITLE: Structure-function analyses of eicosanoid receptors. Physiologic and therapeutic implications
AUTHOR(S): Breyer, Richard M.; Kennedy, Christopher R. J.; Zhang, Yahua; Breyer, Matthew D.
CORPORATE SOURCE: Departments of Medicine (Division of Nephrology), Pharmacology, Vanderbilt University School of Medicine, Nashville, TN, USA
SOURCE: Annals of the New York Academy of Sciences (2000), 905(Lysophospholipids and Eicosanoids in Biology and Pathophysiology), 221-231
CODEN: ANYAA9; ISSN: 0077-8923
PUBLISHER: New York Academy of Sciences
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 35 refs. Prostaglandins (PGs) are ubiquitous lipid mediators derived from cyclooxygenase (COX) metabolism of arachidonic acid that exert a broad range of physiol. activities including modulation of inflammation, ovulation, and arterial blood pressure. The physiol. actions of PGs are mediated in part by their interaction with specific G-protein-coupled PG receptors. Eight PG receptors have been cloned, including four for the major COX metabolite, PGE2. The physiol. roles of the PGE2 receptors have been investigated utilizing subtype-selective agonists, localization of receptor mRNA expression, and creation of mice with targeted disruption of PG receptor genes. These analyses have delineated discrete roles for the various PG receptor subtypes. Recent studies on mice lacking the PGE2 EP2 receptor have implicated the PGE2 EP2 receptor subtype in arterial dilatation and salt-sensitive hypertension, and also indicate that this receptor plays a

key role in female fertility. The EP2 receptor may thus prove to be a productive target for pharmacol. intervention in the treatment of hypertension and infertility.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 14 OF 26 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:593506 HCAPLUS
DOCUMENT NUMBER: 131:309560
TITLE: Abortive expansion of the cumulus and impaired fertility in mice lacking the prostaglandin E receptor subtype EP2
AUTHOR(S): Hizaki, Hiroko; Segi, Eri; Sugimoto, Yukihiko; Hirose, Masaya; Saji, Tomomi; Ushikubi, Fumitaka; Matsuoka, Toshiyuki; Noda, Yoichi; Tanaka, Takashi; Yoshida, Nobuaki; Narumiya, Shuh; Ichikawa, Atsushi
CORPORATE SOURCE: Department of Physiological Chemistry, Faculty of Pharmaceutical Sciences, Kyoto University, Kyoto, 606-8501, Japan
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1999), 96(18), 10501-10506
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Female mice lacking the gene encoding the prostaglandin (PG) E2 receptor subtype EP2 (EP2-/-) become pregnant and deliver their pups at term, but with a much reduced litter size. A decrease in ovulation number and a much reduced fertilization rate were observed in EP2-/- females without difference of the uterus to support implantation of wild-type embryos. Treatment with gonadotropins induced EP2 mRNA expression in the cumulus cells of ovarian follicles of wild-type mice. The immature cumuli oophori from wild-type mice expanded in vitro in response to both FSH and PGE2, but the response to PGE2 was absent in those from EP2-/- mice. Cumulus expansion proceeded normally in preovulatory follicles but became abortive in a number of ovulated complexes in EP2-/- mice, indicating that EP2 is involved in cumulus expansion in the oviduct in vivo. No difference in the fertilization rate between wild-type and EP2-/- mice was found in in vitro studies using cumulus-free oocytes. These results indicate that PGE2 cooperates with gonadotropin to complete cumulus expansion for successful fertilization.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	54.05	65.13

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-6.75	-6.75

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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Nov 3, 2006 (20061103/UP).

=> s ep2 and e1-3
0 EP2
0 "AH"/BI

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             0 "6809"/BI
             0 "AH 6809"/BI
                 (("AH"(W)"6809")/BI)
             0 33458/BI
             3 93/BI
           133 4/BI
             0 33458-93-4/BI
                 ((33458(W)93(W)4)/BI)
            71 "6"/BI
             0 "ISOPROPOXY"/BI
            39 "9"/BI
             0 "OXOXANTHENE"/BI
           199 "2"/BI
             0 "CARBOXYLIC"/BI
             6 "ACID"/BI
             1 "ACIDS"/BI
             6 "ACID"/BI
                 (("ACID" OR "ACIDS")/BI)
             0 "6-ISOPROPOXY-9-OXOXANTHENE-2-CARBOXYLIC ACID"/BI
                 (("6"(W)"ISOPROPOXY"(W)"9"(W)"OXOXANTHENE"(W)"2"(W)"CARBOXYLIC
                 "(W)"ACID")/BI)
L10          0 EP2 AND ("AH 6809"/BI OR 33458-93-4/BI OR "6-ISOPROPOXY-9-OXOXAN
               THENE-2-CARBOXYLIC ACID"/BI)

=> FIL MEDL HCAPL BIOSIS USPATF WPIDS
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
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FULL ESTIMATED COST                                 1.14      66.27

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
                                                   ENTRY    SESSION
CA SUBSCRIBER PRICE                                 0.00      -6.75

FILE 'MEDLINE' ENTERED AT 15:12:22 ON 09 NOV 2006

FILE 'HCAPLUS' ENTERED AT 15:12:22 ON 09 NOV 2006
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FILE 'USPATFULL' ENTERED AT 15:12:22 ON 09 NOV 2006
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FILE 'WPIDS' ENTERED AT 15:12:22 ON 09 NOV 2006
COPYRIGHT (C) 2006 THE THOMSON CORPORATION

=> s ep2 and e1-3
L11        184 EP2 AND ("AH 6809"/BI OR 33458-93-4/BI OR "6-ISOPROPOXY-9-OXOXAN
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=> s ep2 antagonist and e1-3
L12         22 EP2 ANTAGONIST AND ("AH 6809"/BI OR 33458-93-4/BI OR "6-ISOPROPO
               XY-9-OXOXANTHENE-2-CARBOXYLIC ACID"/BI)

=> d ibib abs 20-22

L12  ANSWER 20 OF 22  BIOSIS  COPYRIGHT (c) 2006 The Thomson Corporation  on
     STN
ACCESSION NUMBER:    2003:258857  BIOSIS
DOCUMENT NUMBER:     PREV200300258857
TITLE:               PGE2 constricts porcine large cerebral arteries.
AUTHOR(S):           Jadhav, Vikram [Reprint Author]; Lee, Tony J.-F.
```

CORPORATE SOURCE: Department of Pharmacology, Southern Illinois University School of Medicine, 801 N. Rutledge St, Springfield, IL, 62794-9629, USA
vjadhav@siumed.edu; tlee@siumed.edu
SOURCE: FASEB Journal, (March 2003) Vol. 17, No. 4-5, pp. Abstract No. 147.1. http://www.fasebj.org/. e-file.
Meeting Info.: FASEB Meeting on Experimental Biology: Translating the Genome. San Diego, CA, USA. April 11-15, 2003. FASEB.
ISSN: 0892-6638 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Jun 2003
Last Updated on STN: 4 Jun 2003

AB Prostaglandin E2 (PGE2) has generally been considered a vasodilator. Our preliminary studies, however, demonstrated that PGE2 (1nM-3(M) exclusively contracted isolated porcine large cerebral arteries. The mechanism of action of PGE2 in inducing cerebrovascular contraction was examined using the in vitro tissue bath technique. The PGE2-induced contraction, which was not affected by endothelium denudation or cold-storage denervation of perivascular neurons, was mimicked by 17-phenyl trinor PGE2 and sulprostone (EP1/EP3 receptor agonists). The contraction induced by these agonists and PGE2 was blocked by SC-19220 (a selective EP1 antagonist), AH-6809 (an EP1/EP2 antagonist), and U-73122 and neomycin (phospholipase C inhibitors). It was also observed that prior contraction of these arteries by vasoconstrictors like U-46619 (a thromboxane A2 analog, 0.3(M) or KCl (80mM) significantly potentiated PGE2-and sulprostone-induced contractions, which were attenuated by AH-6809. The enhanced PGE2 response was abolished by combining nifedipine with U-73122. Furthermore, EP1 receptor-immunoreactivities were demonstrated on the smooth muscle in whole-mount arterial preparations. These results suggest that PGE2 induces exclusive contraction of porcine large cerebral arteries, which is mediated by phosphatidyl-inositol pathway via activation of EP1 receptors.

L12 ANSWER 21 OF 22 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:378562 BIOSIS
DOCUMENT NUMBER: PREV200200378562
TITLE: Involvement of TP and EP3 receptors in vasoconstrictor responses to isoprostanes in pulmonary vasculature.
AUTHOR(S): Janssen, Luke J. [Reprint author]; Tazzeo, Tracy
CORPORATE SOURCE: Department of Medicine, McMaster University, St. Joseph's Hospital, 50 Charlton Avenue East, Hamilton, ON, L8N 4A6, Canada
janssenl@mcmaster.ca
SOURCE: Journal of Pharmacology and Experimental Therapeutics, (June, 2002) Vol. 301, No. 3, pp. 1060-1066. print.
CODEN: JPETAB. ISSN: 0022-3565.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Jul 2002
Last Updated on STN: 10 Jul 2002

AB Although isoprostanes generally act on smooth muscle via TXA2-selective prostanoid receptors (TPs), some suggest other prostanoid receptors or possibly even a novel isoprostane-selective receptor might be involved. We studied contractions to several isoprostanes in porcine pulmonary vasculature using organ bath techniques. 8-iso-prostaglandin E2 (PGE2) was the most potent and efficacious of the isoprostanes, with a log EC50 of -7.0+-0.2 in the pulmonary artery and -6.8+-0.2 in the pulmonary vein. The responses to all the isoprostanes were essentially completely blocked by the TP receptor antagonist ICI 192605 (4(Z)-6-((2,4,5-cis)2-(2-chlorophenyl)-4-(2-hydroxy-phenyl)1,3-dioxan-5-yl)hexenoic acid), and the equilibrium dissociation constants for ICI 192605 competing with U46619 or

8-iso-PGE2 were both apprxeq2 nM, indicating that isoprostane-evoked responses involve primarily TP receptors. Only 8-iso-PGE2 was able to evoke substantial contractions in the presence of ICI 192605 and only in the pulmonary vein. The EC50 of these ICI 192605-insensitive responses was -6.1+-0.2. Using a variety of prostanoid agonists, we found the pulmonary vein lacked excitatory PGF2alpha-selective prostanoid receptor (FP) or PGD2-selective prostanoid receptor (DP) but expressed excitatory EP3 receptors. The ICI 192605-insensitive responses to 8-iso-PGE2 were unaffected by the EP1 antagonist SC-19220 (8-chloro-dibenz(b,f)(1,4)oxazepine-10(11H)-carboxy-(2-acetyl) hydrazine; 10-5 M) but were antagonized by the less selective DP/EP1/EP2 antagonist AH6809 (6-isopropoxy-9-oxoxanthene-2-carboxylic acid; 10-5 M) or by cyclopiazonic acid (10-5 M; depletes the internal Ca2+ store). Our data indicate that, whereas 8-iso-PGE2 constricts pulmonary vasculature primarily through TP receptors, a substantial portion of this response is also directed through EP3 receptors or possibly a novel isoprostane receptor.

L12 ANSWER 22 OF 22 USPATFULL on STN

ACCESSION NUMBER:	2004:77196 USPATFULL
TITLE:	Method for fertility control
INVENTOR(S):	Lindenthal, Bernhard, Berlin, GERMANY, FEDERAL REPUBLIC OF Buchmann, Bernd, Hohen Neuendorf, GERMANY, FEDERAL REPUBLIC OF Skuballa, Werner, Berlin, GERMANY, FEDERAL REPUBLIC OF Hegele-Hartung, Christa, Mulheim a. d. Ruhr, GERMANY, FEDERAL REPUBLIC OF
PATENT ASSIGNEE(S):	Schering AG, Berlin, GERMANY, FEDERAL REPUBLIC OF (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004058975	A1	20040325	
APPLICATION INFO.:	US 2003-606289	A1	20030626	(10)

	NUMBER	DATE
PRIORITY INFORMATION:	GB 2002-14802	20020626
	US 2002-414363P	20020930 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	MILLEN, WHITE, ZELANO & BRANIGAN, P.C., 2200 CLARENDON BLVD., SUITE 1400, ARLINGTON, VA, 22201
NUMBER OF CLAIMS:	11
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	4 Drawing Page(s)
LINE COUNT:	1279

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to a method for impairing cumulus expansion and oocyte maturation, the method comprising antagonizing EP2 receptor and/or inhibiting cyclooxygenase COX-2. The invention also relates to the use of a pharmaceutical composition comprising an EP.sub.2 receptor antagonist (optionally with one or more COX inhibitors) for female contraception.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> s l12 not py>2002
L13 2 L12 NOT PY>2002

=> d ibib abs tot

L13 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:435034 HCAPLUS
DOCUMENT NUMBER: 137:150553
TITLE: Involvement of TP and EP3 receptors in vasoconstrictor responses to isoprostanes in pulmonary vasculature
AUTHOR(S): Janssen, Luke J.; Tazzeo, Tracy
CORPORATE SOURCE: Asthma Research Group, Father Sean O'Sullivan Research Centre, Firestone Institute for Respiratory Health, St. Joseph's Hospital, Department of Medicine, McMaster University, Hamilton, ON, L8N 4A6, Can.
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2002), 301(3), 1060-1066
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Although isoprostanès generally act on smooth muscle via TXA2-selective prostanoid receptors (TPs), some suggest other prostanoid receptors or possibly even a novel isoprostane-selective receptor might be involved. The authors studied contractions to several isoprostanes in porcine pulmonary vasculature using organ bath techniques. 8-Iso-prostaglandin E2 (PGE2) was the most potent and efficacious of the isoprostanes, with a log EC50 of -7.0 in the pulmonary artery and -6.8 in the pulmonary vein. The responses to all the isoprostanes were essentially completely blocked by the TP receptor antagonist ICI 192605 [4(Z)-6-[(2,4,5-cis)2-(2-chlorophenyl)-4-(2-hydroxyphenyl)1,3-dioxan-5-yl] hexenoic acid], and the equilibrium dissociation consts. for ICI 192605 competing with U46619 or 8-iso-PGE2 were both ≈2 nM, indicating that isoprostane-evoked responses involve primarily TP receptors. Only 8-iso-PGE2 was able to evoke substantial contractions in the presence of ICI 192605 and only in the pulmonary vein. The EC50 of these ICI 192605-insensitive responses was -6.1. Using a variety of prostanoid agonists, the authors found the pulmonary vein lacked excitatory PGF2α-selective prostanoid receptor (FP) or PGD2-selective prostanoid receptor (DP) but expressed excitatory EP3 receptors. The ICI 192605-insensitive responses to 8-iso-PGE2 were unaffected by the EP1 antagonist SC-19220 [8-chloro-debenz[b,f][1,4]oxazepine-10(11H)-carboxy-(2-acetyl) hydrazine; 10-5 M] but were antagonized by the less selective DP/EP1/EP2 antagonist AH6809 (6-isopropoxy-9-oxoxanthene-2-carboxylic acid; 10-5 M) or by cyclopiazonic acid (10-5 M; depletes the internal Ca2+ store). The authors' data indicate that, whereas 8-iso-PGE2 constricts pulmonary vasculature primarily through TP receptors, a substantial portion of this response is also directed through EP3 receptors or possibly a novel isoprostane receptor.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 2 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:378562 BIOSIS
DOCUMENT NUMBER: PREV200200378562
TITLE: Involvement of TP and EP3 receptors in vasoconstrictor responses to isoprostanes in pulmonary vasculature.
AUTHOR(S): Janssen, Luke J. [Reprint author]; Tazzeo, Tracy
CORPORATE SOURCE: Department of Medicine, McMaster University, St. Joseph's Hospital, 50 Charlton Avenue East, Hamilton, ON, L8N 4A6, Canada
janssenl@mcmaster.ca
SOURCE: Journal of Pharmacology and Experimental Therapeutics, (June, 2002) Vol. 301, No. 3, pp. 1060-1066. print.
CODEN: JPETAB. ISSN: 0022-3565.
DOCUMENT TYPE: Article
LANGUAGE: English

ENTRY DATE: Entered STN: 10 Jul 2002
Last Updated on STN: 10 Jul 2002

AB Although isoprostanes generally act on smooth muscle via TXA2-selective prostanoid receptors (TPs), some suggest other prostanoid receptors or possibly even a novel isoprostane-selective receptor might be involved. We studied contractions to several isoprostanes in porcine pulmonary vasculature using organ bath techniques. 8-iso-prostaglandin E2 (PGE2) was the most potent and efficacious of the isoprostanes, with a log EC50 of -7.0+-0.2 in the pulmonary artery and -6.8+-0.2 in the pulmonary vein. The responses to all the isoprostanes were essentially completely blocked by the TP receptor antagonist ICI 192605 (4(Z)-6-((2,4,5-cis)2-(2-chlorophenyl)-4-(2-hydroxy-phenyl)1,3-dioxan-5-yl)hexenoic acid), and the equilibrium dissociation constants for ICI 192605 competing with U46619 or 8-iso-PGE2 were both apprxeq2 nM, indicating that isoprostane-evoked responses involve primarily TP receptors. Only 8-iso-PGE2 was able to evoke substantial contractions in the presence of ICI 192605 and only in the pulmonary vein. The EC50 of these ICI 192605-insensitive responses was -6.1+-0.2. Using a variety of prostanoid agonists, we found the pulmonary vein lacked excitatory PGF2alpha-selective prostanoid receptor (FP) or PGD2-selective prostanoid receptor (DP) but expressed excitatory EP3 receptors. The ICI 192605-insensitive responses to 8-iso-PGE2 were unaffected by the EP1 antagonist SC-19220 (8-chloro-debenz(b,f)(1,4)oxazepine-10(11H)-carboxy-(2-acetyl) hydrazine; 10-5 M) but were antagonized by the less selective DP/EP1/EP2 antagonist AH6809 (6-isopropoxy-9-oxoxanthene-2-carboxylic acid; 10-5 M) or by cyclopiazonic acid (10-5 M; depletes the internal Ca2+ store). Our data indicate that, whereas 8-iso-PGE2 constricts pulmonary vasculature primarily through TP receptors, a substantial portion of this response is also directed through EP3 receptors or possibly a novel isoprostane receptor.

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=> s ep2 (S) e1-3
L14          92 EP2 (S) ("AH 6809"/BI OR 33458-93-4/BI OR "6-ISOPROPOXY-9-OXOXAN
                THENE-2-CARBOXYLIC ACID"/BI)

=> s l14 not py>2002
L15          37 L14 NOT PY>2002

=> focus
PROCESSING COMPLETED FOR L15
L16          37 FOCUS L15 1-

=> d ibib abs 1-5

L16  ANSWER 1 OF 37  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         1995:981657  HCAPLUS
DOCUMENT NUMBER:          124:77225
TITLE:                    6-Isopropoxy-9-
                          oxoxanthene-2-carboxylic
                          acid (AH 6809), a human
                          EP2 receptor antagonist
AUTHOR(S):                Woodward, David F.; Pepperl, David J.; Burkey, Thomas
                          H.; Regan, John W.
CORPORATE SOURCE:         Biol. Sci., Allergan, Inc., Irvine, CA, 92713, USA
SOURCE:                   Biochemical Pharmacology (1995), 50(10), 1731-3
                          CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER:                Elsevier
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB  On studying the interaction of various ligands with the pharmacol.
    defined, recombinant human EP2 receptor (J. W. Regan et al.,
    1994), the authors discovered that the putative EP1 receptor antagonist
    6-isopropoxy-9-oxoxanthene-2
```

-carboxylic acid (AH 6809) also
has affinity for the human EP2 receptor. Moreover, AH
6809 behaved as an EP2 receptor antagonist and inhibited
prostaglandin E2 (PGE2)-stimulated increases in cAMP formation in COS-7
cells transfected with the human EP2 receptor. These findings
have significant implications for studies that employ AH 6809 to determine the
pharmacol. basis of PGE2-induced responses in human cells and tissues.

L16 ANSWER 2 OF 37 MEDLINE on STN
ACCESSION NUMBER: 96095732 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7503778
TITLE: 6-Isopropoxy-9-
oxoxanthene-2-carboxylic
acid (AH 6809), a human
EP2 receptor antagonist.
AUTHOR: Woodward D F; Pepperl D J; Burkey T H; Regan J W
CORPORATE SOURCE: Department of Biosciences (RD-2C), Allergan Inc., Irvine, CA 92713, USA.
SOURCE: Biochemical pharmacology, (1995 Nov 9) Vol. 50, No. 10, pp. 1731-3.
Journal code: 0101032. ISSN: 0006-2952.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199601
ENTRY DATE: Entered STN: 17 Feb 1996
Last Updated on STN: 3 Feb 1997
Entered Medline: 17 Jan 1996
AB On studying the interaction of various ligands with the pharmacologically defined, recombinant human EP2 receptor (Regan et al., Mol Pharmacol 46: 213-220, 1994), we discovered that the putative EP1 receptor antagonist 6-isopropoxy-9-
oxoxanthene-2-carboxylic acid (
AH 6809) also has affinity for the human EP2
receptor. Moreover, AH 6809 behaved as an EP2
receptor antagonist and inhibited prostaglandin E2 (PGE2)-stimulated increases in cyclic AMP. These findings have significant implications for studies that employ AH 6809 to determine the pharmacological basis of PGE2-induced responses in human cells and tissues.

L16 ANSWER 3 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:435034 HCAPLUS
DOCUMENT NUMBER: 137:150553
TITLE: Involvement of TP and EP3 receptors in vasoconstrictor responses to isoprostanes in pulmonary vasculature
AUTHOR(S): Janssen, Luke J.; Tazzeo, Tracy
CORPORATE SOURCE: Asthma Research Group, Father Sean O'Sullivan Research Centre, Firestone Institute for Respiratory Health, St. Joseph's Hospital, Department of Medicine, McMaster University, Hamilton, ON, L8N 4A6, Can.
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2002), 301(3), 1060-1066
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Although isoprostanes generally act on smooth muscle via TXA2-selective prostanoid receptors (TPs), some suggest other prostanoid receptors or possibly even a novel isoprostane-selective receptor might be involved. The authors studied contractions to several isoprostanes in porcine pulmonary vasculature using organ bath techniques. 8-Iso-prostaglandin E2 (PGE2) was the most potent and efficacious of the isoprostanes, with a log EC50 of -7.0 in the pulmonary artery and -6.8 in the pulmonary vein. The

responses to all the isoprostanes were essentially completely blocked by the TP receptor antagonist ICI 192605 [4(Z)-6-[(2,4,5-cis)2-(2-chlorophenyl)-4-(2-hydroxyphenyl)1,3-dioxan-5-yl] hexenoic acid], and the equilibrium dissociation consts. for ICI 192605 competing with U46619 or 8-iso-PGE2 were both ≈2 nM, indicating that isoprostane-evoked responses involve primarily TP receptors. Only 8-iso-PGE2 was able to evoke substantial contractions in the presence of ICI 192605 and only in the pulmonary vein. The EC50 of these ICI 192605-insensitive responses was -6.1. Using a variety of prostanoid agonists, the authors found the pulmonary vein lacked excitatory PGF2α-selective prostanoid receptor (FP) or PGD2-selective prostanoid receptor (DP) but expressed excitatory EP3 receptors. The ICI 192605-insensitive responses to 8-iso-PGE2 were unaffected by the EP1 antagonist SC-19220 [8-chloro-debenz[b,f][1,4]oxazepine-10(11H)-carboxy-(2-acetyl) hydrazine; 10-5 M] but were antagonized by the less selective DP/EP1/EP2 antagonist AH6809 (6-isopropoxy-9-oxoxanthene -2-carboxylic acid; 10-5 M) or by cyclopiazonic acid (10-5 M; depletes the internal Ca2+ store). The authors' data indicate that, whereas 8-iso-PGE2 constricts pulmonary vasculature primarily through TP receptors, a substantial portion of this response is also directed through EP3 receptors or possibly a novel isoprostane receptor.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 37 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:378562 BIOSIS
DOCUMENT NUMBER: PREV200200378562
TITLE: Involvement of TP and EP3 receptors in vasoconstrictor responses to isoprostanes in pulmonary vasculature.
AUTHOR(S): Janssen, Luke J. [Reprint author]; Tazzeo, Tracy
CORPORATE SOURCE: Department of Medicine, McMaster University, St. Joseph's Hospital, 50 Charlton Avenue East, Hamilton, ON, L8N 4A6, Canada
janssenl@mcmaster.ca
SOURCE: Journal of Pharmacology and Experimental Therapeutics, (June, 2002) Vol. 301, No. 3, pp. 1060-1066. print.
CODEN: JPETAB. ISSN: 0022-3565.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Jul 2002
Last Updated on STN: 10 Jul 2002

AB Although isoprostanes generally act on smooth muscle via TXA2-selective prostanoid receptors (TPs), some suggest other prostanoid receptors or possibly even a novel isoprostane-selective receptor might be involved. We studied contractions to several isoprostanes in porcine pulmonary vasculature using organ bath techniques. 8-iso-prostaglandin E2 (PGE2) was the most potent and efficacious of the isoprostanes, with a log EC50 of -7.0+-0.2 in the pulmonary artery and -6.8+-0.2 in the pulmonary vein. The responses to all the isoprostanes were essentially completely blocked by the TP receptor antagonist ICI 192605 (4(Z)-6-((2,4,5-cis)2-(2-chlorophenyl)-4-(2-hydroxy-phenyl)1,3-dioxan-5-yl)hexenoic acid), and the equilibrium dissociation constants for ICI 192605 competing with U46619 or 8-iso-PGE2 were both apprxeq2 nM, indicating that isoprostane-evoked responses involve primarily TP receptors. Only 8-iso-PGE2 was able to evoke substantial contractions in the presence of ICI 192605 and only in the pulmonary vein. The EC50 of these ICI 192605-insensitive responses was -6.1+-0.2. Using a variety of prostanoid agonists, we found the pulmonary vein lacked excitatory PGF2alpha-selective prostanoid receptor (FP) or PGD2-selective prostanoid receptor (DP) but expressed excitatory EP3 receptors. The ICI 192605-insensitive responses to 8-iso-PGE2 were unaffected by the EP1 antagonist SC-19220 (8-chloro-debenz(b,f)(1,4)oxazepine-10(11H)-carboxy-(2-acetyl) hydrazine; 10-5 M) but were antagonized by the less selective DP/EP1/EP2 antagonist

AH6809 (6-isopropoxy-9-oxoxanthene
-2-carboxylic acid; 10-5 M) or by
cyclopiazonic acid (10-5 M; depletes the internal Ca2+ store). Our data indicate that, whereas 8-iso-PGE2 constricts pulmonary vasculature primarily through TP receptors, a substantial portion of this response is also directed through EP3 receptors or possibly a novel isoprostane receptor.

L16 ANSWER 5 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:216423 HCAPLUS
DOCUMENT NUMBER: 135:29379
TITLE: Prostaglandin E2 increases cyclic AMP and inhibits endothelin-1 production/secretion by guinea-pig tracheal epithelial cells through EP4 receptors
AUTHOR(S): Pelletier, Stephane; Dube, Jean; Villeneuve, Annie; Gobeil, Fernand, Jr.; Yang, Quan; Battistini, Bruno; Guillemette, Gaetan; Sirois, Pierre
CORPORATE SOURCE: Institut de Pharmacologie de Sherbrooke, Universite de Sherbrooke, Sherbrooke, QC, J1H 5N4, Can.
SOURCE: British Journal of Pharmacology (2001), 132(5), 999-1008
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Prostaglandin E2 (PGE2) increased cAMP formation in tracheal epithelial cells and concomitantly decreased the production/secretion of immunoreactive endothelin (irET). Naturally occurring prostanoids and selective and non-selective EP receptor agonists showed the following rank order of potency in stimulating cAMP generation by epithelial cells: PGE2 (EP-selective) > 16,16-dimethyl PGE2 (EP-selective) > 11-deoxy PGE2 (EP-selective) >>> iloprost (IP/EP1/EP3-selective), butaprost (EP2-selective), PGD2 (DP-selective), PGF2α (FP-selective). The lack of responsiveness of the latter prostanoids indicated that the prostanoid receptor present in these cells is not of the DP, FP, IP, EP1, EP2 or EP3 subtype. Preincubating the cells with the selective TP/EP4-receptor antagonists AH 23848B and AH 22921X antagonized the PGE2-evoked cAMP generation. This suggested that EP4 receptors mediate PGE2 effects. However, in addition to any antagonistic effects at EP4-receptors, both compds., to a different extent, modified cAMP metabolism The selective EP1, DP and EP2 receptor antagonist (AH 6809) failed to inhibit PGE2-evoked cAMP generation which confirmed that the EP2 receptor subtype did not contribute to the change in cAMP formation in these cells. The PGE2-induced inhibition of irET production by guinea pig tracheal epithelial cells was due to cAMP generation and activation of the cAMP-dependent protein kinase since this effect was reverted by the cAMP antagonist Rp-cAMPS. These results provide the first evidence supporting the existence of a functional prostaglandin E2 receptor that shares the pharmacol. features of the EP4-receptor subtype in guinea pig tracheal epithelial cells. These receptors modulate cAMP formation as well as ET-1 production/secretion in these cells.
REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l15 36-37 ibib abs

L15 ANSWER 36 OF 37 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2000:216884 BIOSIS
DOCUMENT NUMBER: PREV200000216884
TITLE: Characterization of prostanoid receptors mediating inhibition of histamine release from anti-IgE-activated rat peritoneal mast cells.

AUTHOR(S): Chan, C. L.; Jones, R. L.; Lau, H. Y. A. [Reprint author]
CORPORATE SOURCE: Department of Pharmacology, Faculty of Medicine, Chinese University of Hong Kong, Shatin, Basic Medical Sciences Building, New Territories, Hong Kong, China
SOURCE: British Journal of Pharmacology, (Feb., 2000) Vol. 129, No. 3, pp. 589-597. print.
CODEN: BJPCBM. ISSN: 0007-1188.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 31 May 2000
Last Updated on STN: 5 Jan 2002

AB 1. Prostanoid receptors mediating inhibition of anti-IgE induced histamine release from rat peritoneal mast cells have been characterized pharmacologically. PGD2 and the specific DP receptor agonists BW 245C and ZK 118182 were the most potent inhibitors with half-maximal concentrations of 0.26, 0.06 and 0.02 muM respectively. The maximum inhibition attainable was 60-65% with 10-5 M BW 245C and ZK 118182. 2. Among several EP receptor agonists investigated, only PGE2 and the EP2/EP3 receptor agonist misoprostol induced significant inhibition (46.8 +- 4.7% at 10-4 M and 18.7 +- 6.8% at 10-5 M respectively). The IP receptor agonists cicaprost and iloprost were both less potent than the DP agonists in inhibiting histamine release (45.2 +- 3.3% and 35.1 +- 2.5% inhibition respectively at 10-5 M), whereas PGF2alpha and the TP receptor agonist U-46619 were only marginally effective. 3. The EP4/TP receptor antagonist AH 23848 failed to affect the inhibitory actions of PGD2 or PGE2 even at 10-5 M, whereas the DP/EP1/EP2 receptor antagonist AH 6809 slightly enhanced the effect of PGD2 at 10-6 M. 4. At concentrations of 3 X 10-6 to 10-5 M, the putative DP receptor antagonist ZK 138357 dose-dependently suppressed the inhibitory activities of the DP agonists, PGE2 and cicaprost. The antagonism of ZK 138357 against the DP receptor agonists appeared to be competitive with pA2 values of around six. 5. In conclusion, these data support our earlier proposal that an inhibitory DP receptor is the predominant prostanoid receptor in rat peritoneal mast cell. The properties of this receptor in relation to putative DP receptor subtypes reported in the literature are discussed.

L15 ANSWER 37 OF 37 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1992:284401 BIOSIS
DOCUMENT NUMBER: PREV199294009051; BA94:9051
TITLE: INVESTIGATION OF THE PROSTAGLANDIN E EP-RECEPTOR SUBTYPE MEDIATING RELAXATION OF THE RABBIT JUGULAR VEIN.
AUTHOR(S): LAWRENCE R A [Reprint author]; JONES R L
CORPORATE SOURCE: DEP PHARMACOL, FAC MED, CHINESE UNIV OF HONG KONG, SHATIN, NT, HONG KONG
SOURCE: British Journal of Pharmacology, (1992) Vol. 105, No. 4, pp. 817-824.
CODEN: BJPCBM. ISSN: 0007-1188.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 10 Jun 1992
Last Updated on STN: 10 Jun 1992

AB 1 Prostaglandin E2 (PGE2) relaxes circular smooth muscle of the rabbit isolated jugular vein at very low concentrations (mean pIC50 against histamine-induced contraction = 9.34). This effect is not blocked by the EP1-receptor antagonist, AH 6809 (2 μM). 2 From a group of prostaglandin E analogues examined, 16,16-dimethyl PGE2, misoprostol, 11-deoxy PGE2-1-alcohol and 11-deoxy PGE1 were highly potent relaxant agents, whereas 17-phenyl-ω-trinor PGE2, MB 28767 and butaprost had low potency and sulprostone and oxoprostol were virtually inactive. 3 Comparison of the jugular vein data with published data for inhibitory agonist potencies on the cat trachea (EP2 preparation) and the field-stimulated guinea-pig vas deferens (EP3) indicates that the EP-receptor in the rabbit jugular vein is closest to

the EP2 subtype. However, the correlation is not entirely convincing. For example, butaprost, 16,16-dimethyl PGE2 and 11-deoxy PGE1 are of similar potency on the cat trachea, whereas butaprost is about 300 times less potent than the other two analogues on the jugular vein. The existence of more than one EP2-receptor appears possible. 4 It was felt that the activity of butaprost required further investigation in view of the claim that it is a specific EP2-receptor agonist. We have shown that butaprost has very low inhibitory activity on the guinea-pig vas deferens, a very sensitive EP3-receptor containing preparation. However, on the chick ileum, the original EP3 preparation, butaprost showed potent contractile activity (pEC25 .apprx. 8.0). In addition, its maximum response was lower than that of PGE2; lower maxima were also found for sulprostone, MB 28767 and oxoprostol, but not for ICI 80205, 16,16-dimethyl PGE2 and 17-phenyl-ω-trinor PGE2. The maximal response to a combination of either sulprostone and butaprost or sulprostone and PGE2 was similar to that achieved by PGE2 alone. Analysis of the interaction between sulprostone and PGE2 appears to exclude a partial agonist action for sulprostone. Furthermore neither sulprostone nor butaprost appear to have inhibitory activity on the ileum. AH 6809 at 2 μM produced only a small shift of the PGE2 log concentration-response curve. 5 It is likely that contraction of the longitudinal smooth muscle of the chick ileum is mediated by (at least) two EP-receptor subtypes; activation of only one receptor system does not induce the maximum response (i.e. the acetylcholine maximum) of the preparation. One receptor could be an EP3 subtype, at which sulprostone exerts a selective agonist action. The other receptor is unlikely to be an EP1 subtype, because of the high agonist potency of butaprost, the low agonist potency of iloprost, and the low antagonist potency of AH 6809. An alternative hypothesis is that the chick ileum contains a novel EP-receptor subtype in addition to an EP3-receptor.

=>

---Logging off of STN---

Connection closed by remote host
END

Unable to generate the STN prompt.
Exiting the script...